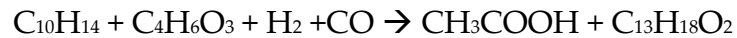


ASPENPLUS™

Example - Semi-Batch production of Ibuprofen

Problem Statement:

Ibuprofen is produced from the reactants isobutylbenzene, acetic anhydride, hydrogen, and carbon monoxide. The overall reaction is defined as



with an estimated kinetic rate expression of

$$r_{\text{IBU}} = k[\text{C}_{10}\text{H}_{14}]^2[\text{C}_4\text{H}_6\text{O}_3][\text{H}_2][\text{CO}]$$

where $k = 0.349 \text{ m}^{12}/\text{mol}^3\cdot\text{s}$. As with many pharmaceuticals, the production of Ibuprofen is carried out in a semi-batch reactor. A 2 m^3 reactor is charged with equal molar amounts of isobutylbenzene and acetic anhydride. The reactor is pressurized to $1.4 \text{ e}7 \text{ Pa}$ with equal molar hydrogen and carbon monoxide gas at $4 \text{ e-}2 \text{ kg/s}$. All components are heated to 410 K before being introduced into the system, where the temperature is held constant.

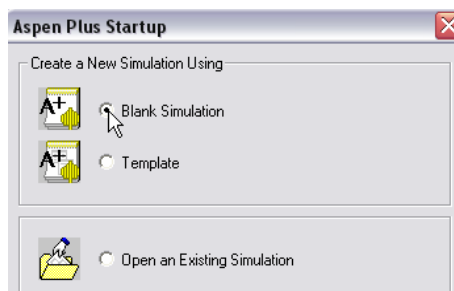
Determine the amount of time required to achieve a conversion of 90% with respect to isobutylbenzene.


Method of Solution:

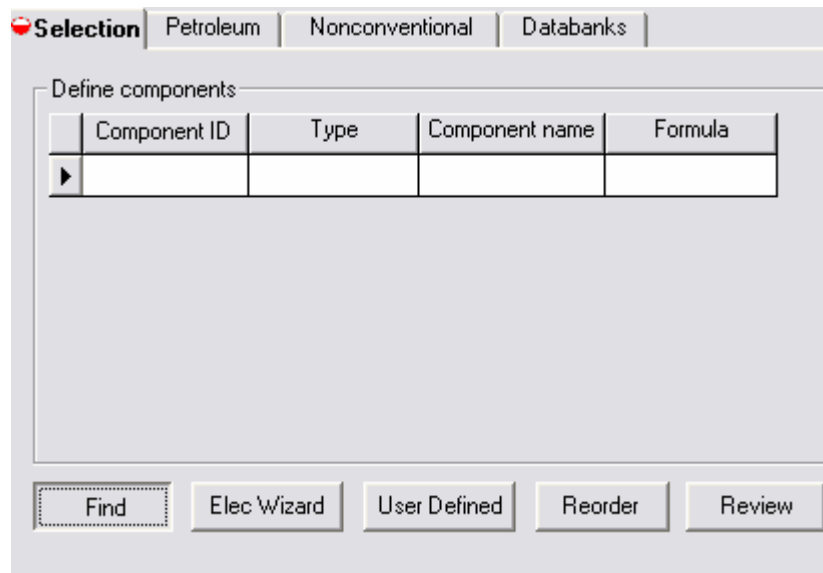
Use the RBATCH unit in AspenPlus to simulate the semi-batch process.

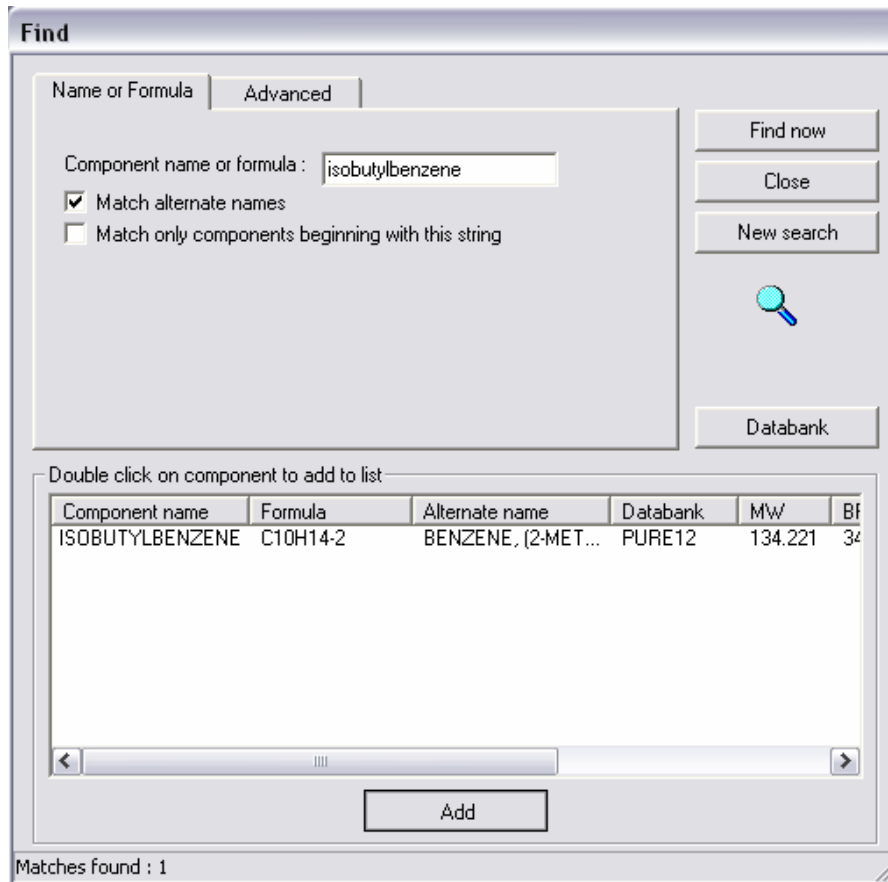
Solution:

- 1) Open the Aspen Plus™ program. [For most computers, from the START menu: Start/Programs/AspenTech/Aspen Engineering Suite/Aspen Plus 12.1/Aspen Plus User Interface]
- 2) Select “Blank Simulation” and click **OK**.



- 3) If necessary, be sure that the program has a connection to an appropriate server and can access the software license (Local PC).
- 4) Eventually, the *Process Flowsheet Window* should appear.
- 5) Open the *Data Browser* by clicking on the  icon on the toolbar. First, add the system components. Click on the **Components** section of the *Data Browser*.
- 6) On the Selection tab click **Find**. The *Find* window will appear. Type "Isobutylbenzene" and click **Find now**. Select ISOBUTYLBENZENE and click **Add**. Add the remaining components in the same fashion. If you add a component by mistake, close the *Find* window, right-click on the row to delete and select delete row from the drop down menu.





7) The component list should resemble the figure below.

Define components

Component ID	Type	Component name	Formula
ISOBU-01	Conventional	ISOBUTYLBENZENE	C10H14-2
ACETI-01	Conventional	ACETIC-ANHYDRIDE	C4H6O3
HYDRO-01	Conventional	HYDROGEN	H2
CARBO-01	Conventional	CARBON-MONOXIDE	CO
ACETI-02	Conventional	ACETIC-ACID	C2H4O2-1
IBUPR-01	Conventional	IBUPROFEN	C13H18O2
*			

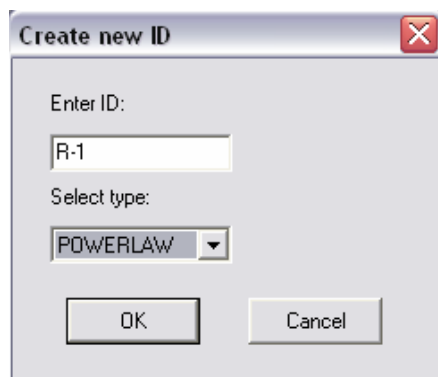
8) Next, specify the property package that Aspen Plus™ will use to define the system. Open the **Properties** section by clicking on the folder. Click on **Specifications**.



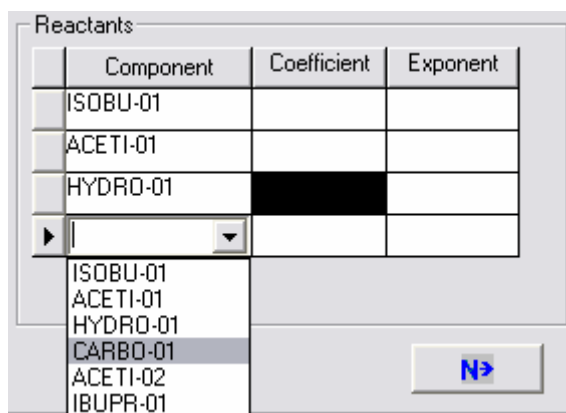
9) On the Global tab, under Base method, select *Wilson*. The remaining options will update.

10) The reaction must also be defined. Open the **Reactions** folder. Click on the **Reactions** subfolder. In the *Object manager* click **New...**

11) In the pop-up window. Select the type as **POWERLAW**.



- 12) Click **OK**. Another subfolder is reacted for that reaction set. On the stoichiometry tab, click **New...** Be sure that the Reaction type is set in **Kinetic**. Add reactants by selecting the correct chemicals Component in the Reactants section.



- 13) Add the products in the same fashion, only in the Products section. Define the stoichiometric coefficients in the Coefficient column. Use negatives for reactants and positives for products. In the Exponent column, enter the corresponding power defined in the rate law. If a component is not factored into the rate law, leave the Exponent column empty. (the default is 0)

Reaction No.: Reaction type:

Reactants			
Component	Coefficient	Exponent	
ISOBU-01	-1	2	
ACETI-01	-1	1	
HYDRO-01	-1	1	
CARBO-01	-1	1	

Products			
Component	Coefficient	Exponent	
ACETI-02	1		
IBUPR-01	1		
*			

- 14) Click the Next button. Select the Kinetic tab. Set the Reacting phase as **Liquid** and the [Ci] basis to **Molarity**. Only k needs to be defined. The remaining data is figured into that value. Enter **0.349** as k. Aspen Plus requires that an activation energy be defined. Enter **0** for E.

Stoichiometry
 Kinetic
 Equilibrium

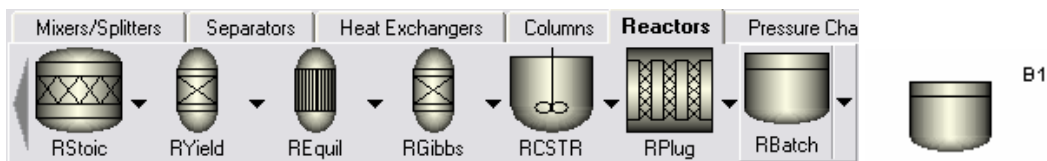
1) ISOBU-01 + ACETI-01 + HYDRO-01 + CARBO-01 -> ACETI-02 + IBUPR-01

Reacting phase:

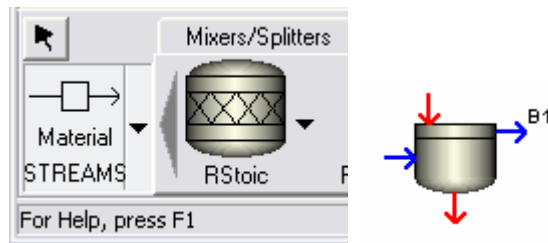
Power Law kinetic expression
 Kinetic factor = $k(T/T_0)^n e^{-E/R(1/T-1/T_0)}$


k:
 n:
 E: J/kmol
 To: K
 [Ci] basis:

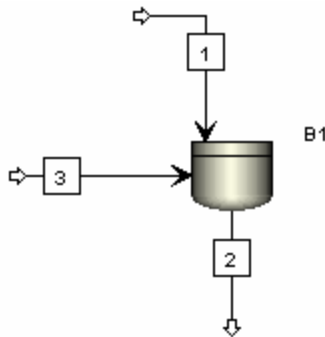
- 15) Next, the PFD must be set up. Close the **Data Browser**. From the **Process Equipment Library** click on the Reactors tab. Click on **RBatch** and click again on the Process Flowsheet to add the reactor.



- 16) The RBatch unit requires that you define an inlet and an outlet. In the **Stream Library**, click on **Materials STREAMS**. Hover the cursor over the PFD to view the possible connections. Required connections are red, while optional connections are blue.



- 17) Add the required inlet stream by click on the PFD above the reactor and again on the top red arrow. Add the required outlet stream by click on the lower red arrow and again below the reactor on the PFD. Add a third optional inlet in the same fashion. When finished added anything to the PFD, select the arrow icon, , to avoid adding unwanted operations.



- 18) In the figure above, stream 1 is used to define the batch charge, stream 2 is used to hold the results from the batch reactor, and stream 3 is used to define continuous feeds.
- 19) Next we will define the batch charge. Double click on Stream 1. The data browser should open. Set the Temperature to 410 K, the Pressure at 101325 Pa, and Total flow as 2 m³/sec. Change the flow units by using the drop-down menu in the box above the units. Change the Composition units to Mole-Frac and enter a value of 0.5 for both ISOBU-01 (isobutylbenzene) and ACETI-01 (acetic anhydride).

Specifications | Flash Options | PSD | Component Attr. | EO Options

Substream name: MIXED Ref Temperature

State variables:

Temperature: 410 K

Pressure: 101325 N/sqm

Total flow: Volume 2 cum/sec

Solvent:

Composition:

Mole-Frac

Component	Value
ISOBU-01	0.5
ACETI-01	0.5
HYDRO-01	
CARBO-01	
ACETI-02	
IBUPR-01	

Total: 1

- 20) Next we will define the H₂ and CO continuous feed stream. Open the **Stream** subfolder '3' in the *Data Browser*. Set the Temperature as 410 K, the Pressure at 14000000 Pa, and Total flow to 0.04 kg/s. Change the Composition units to Mole-Frac and enter a value of 0.5 for both HYDRO-01 (hydrogen) and CARBO-01 (carbon monoxide).

Specifications | Flash Options | PSD | Component Attr. | EO Options

Substream name: MIXED Ref Temperature

State variables:

Temperature: 410 K

Pressure: 14000000 N/sqm

Total flow: Mass 0.04 kg/sec

Solvent:

Composition:

Mole-Frac

Component	Value
ISOBU-01	
ACETI-01	
HYDRO-01	0.5
CARBO-01	0.5
ACETI-02	
IBUPR-01	

Total: 1

- 21) Open the **Blocks** folder to define the reactor. Open the subfolder, **B1**. On the Specifications tab, under Reactor operating specifications, select **Constant Temperature** from the drop-down menu. Specify the Temperature as 410 K. Under Pressure specification, set the Reactor pressure to 14000000. Under Valid phases, select **Vapor-Liquid** for the Reactor.

Specifications
 Reactions
 Stop Criteria
 Operation Times
 Continuous Feeds

Reactor operating specification
 Constant temperature

Temperature: 410 K

Pressure specification
 Specify reactor pressure

Reactor pressure: 14000000 N/sqm

Valid phases
 Reactor: Vapor-Liquid
 Vent accumulator: Vapor-Only

2nd Liquid

- 22) Click on the Reactions tab. Select **R-1** from the Available reaction sets and click the greater than symbol, **>**.
- 23) Click on the Stop Criteria tab. Define the Criterion no. as **1**, the Location as **Reactor**, the Variable type as **Conversion**, the Stop value as 0.9, the Component as **ISOBU-01**, and Approach from **Below**.

Specifications
 Reactions
 Stop Criteria
 Operation Times
 Continuo

Stop criteria

Criterion no.	1	
Location	Reactor	
Variable type	Conversion	
Stop value	0.9	
Component	ISOBU-01	
Substream	MIXED	
Property set ID		
Approach from	Below	

- 24) Click on the Operation Times tab. Select the Batch feed time radio button. Because the batch feed rate is $2 \text{ m}^3/\text{s}$ and the reactor specified as a 2 m^3 reactor, set the Batch feed time as **1 sec**. For the Profile result time, set the Maximum calculation time to 24 hr, and the Time interval between profile points to 0.5 hr

Specifications
 Reactions
 Stop Criteria
 Operation Times
 Continuous Feeds
 ◀ ▶

Batch cycle time

Total cycle time: [] sec ▼

Batch feed time: 1 sec ▼

Down time: 0 sec ▼

Profile result time

Maximum calculation time: 86400 sec ▼

Time interval between profile points: 1800 sec ▼

Maximum number of profile points: 50 ▲▼

25) Click on the Continuous Feeds tab. Stream 3 is already defined.

Stop Criteria
 Operation Times
 Continuous Feeds
 Controllers

Continuous feed mass flow


Stream: 3 ▼

Flow is constant at inlet value

Specify flow vs time profile

	Time	Flow
*		

26) The system has been defined. Press F5 to run the simulation.

27) Click on Control Panel icon, . This provides a set by set printout of the run.

28) Click back to the Data Browser. The **Results Summary** does not provide a good summary for the RBatch unit.

29) Open the **Blocks** folder. Open the **B1** subfolder. Click on **Results**. The reaction time was 5389 sec.

Summary	Balance	Distributions	Polymer Attributes
RBatch results			
Stop criterion number:	1		
Reaction time:	5388.57264	sec	▼
Heat load per cycle:	-1.249E+09	J	▼
Reactor minimum temperature:	410	K	▼
Reactor maximum temperature:	410.062239	K	▼
Maximum volume deviation:			
Maximum volume deviation time:			▼

30) Click on **Profiles** to view a more complete analysis of the system

Results/Considerations:

Aspen Plus™ calculated a run time of 89.8 minutes to achieve a conversion of 90%. This is consistent with typical pharmaceutical batch systems, though it should be noted that the rate equation and rate constant have not been verified with experimental data. Also, with some pharmaceuticals, products take weeks to manufacture, as they require multiple batch cycles.